Protein preserves delicate balance between immune response and host

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The immune system possesses a highly effective arsenal of cellular and chemical weapons that stand ready to defend us from harmful pathogens. However, these same mechanisms that are designed for protection can sometimes wreak havoc on our own body. Now, new research published by Cell Press in the Oct. 29 issue of the journal *Immunity*, provides insight into the mechanisms that regulate natural checks and balances that optimize the immune response against potential threats while preserving host tissues.

White blood cells called neutrophils are part of the body's first line of defense against bacterial infection. Neutrophils are recruited from the bloodstream to infected tissues where they release powerful chemicals that kill bacteria and amplify the immune response. These cells function as first responders at the scene of infection and often have a short life span. As a result, new neutrophils are produced continuously from stem cells in the bone marrow. Previous research has suggested that regulation of neutrophil production is a complex and carefully controlled process.

"We know that the protein CEACAM1 is involved in the regulation of white blood cells, but its specific role in neutrophil-dependent host immune responses has not been investigated," explains senior study author, Dr. John E. Shively from the Beckman Research Institute of City of Hope in Duarte, California. "We were interested in determining what would happen to neutrophil-mediated immunity in mice that did not express CEACAM1." Dr. Shively and coauthor Dr. Hao Pan found that mice lacking CEACAM1 had an excess number of neutrophils and that

CEACAM1 inhibited a specific signaling pathway that is required for white blood cell proliferation.

Interestingly, the excess neutrophils did not provide any additional protection from bacterial infection. In contrast, after infection with *Listeria*, mice without CEACAM1 died dramatically faster than control mice. The researchers went on to show that the mice lacking CEACAM1 exhibited improved bacterial clearance, but that this was accompanied by severe tissue damage to the liver. The authors concluded that the combination of high levels of neutrophil-secreted chemicals damaged the liver and induced accelerated mortality in *Listeria*-infected mice lacking CEACAM1. "The insights from our work highlight the importance of natural mechanisms that restrain white blood cell proliferation and may have clinical implications in treating infectious and auto-inflammatory disorders," says Dr. Shively.

Provided by Cell Press